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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,132	12/06/2006	Susanne Kartin Pedersen	133119.00501	5551

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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	PAPER NUMBER
1645	

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12/07/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,132	PEDERSEN ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 204-223* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 204-223* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/22/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Acknowledgment and entry of the Amendment submitted on is made. Claims 1 and new claims 204-223 are currently pending.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1 and 204-223 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and confusing because it is drawn to identifying 'an immunogenic protein or fragment thereof' by obtaining it from a subject and then identifying the protein which is part of the complex with the goal of 'thereby identifying an immunogenic protein or fragment thereof capable of eliciting an immune response. This method as currently written is extremely vague and confusing. By virtue that the protein was isolated as part of an antibody-antigen complex it would already be known that the protein or fragment thereof could elicit an immune response. Further, how is the protein or fragment identified? What method steps are used for the identification? Additionally, how is the complex itself isolated? How can one of skill in the art go about determining the protein's source or other information? Does this encompass identifying only known proteins or proteins yet to be discovered? It appears to encompass the

latter and it is unclear how one would identify these unknown proteins. Accordingly, the method set forth in the claims is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 204-215 and 217-223 are rejected under 35 U.S.C. 102(b) as being anticipated by (US 5,116,766).

The reference relates to immune complex isolation and methods for diagnosing diseases. See abstract. Column 1 of the patent teaches that it was known to isolate circulating immune complexes from sera by contacting the sera with a component that binds to the immune complexes and may be removed with them. A reagent RhC is used to precipitate the immune complexes from serum. The immune complex with RhC can then be immobilized on a protein A column. The complexes are then eluted using glycine. The antigens are separated by SDS-PAGE electrophoresis and an antigen 'profile' may be generated. See "isolation of IC [Immune Complexes] bridging columns 9-10. See column 7, line 59-column 8, line 16 and Example 2. This clearly teaches obtaining an immune complex from a subject that has been elicited against said portien,

and identifying it. It has already demonstrated that said protein is capable of raising an immune response as there is an antibody directed against it.

Response to Applicant's arguments:

Applicants argue that the reference only provides an invitation to experiment. They argue that "conventional wisdom" in the art led one to believe that proteins would degrade rapidly during infection and not remain intact upon separation from immunoglobulin. This has been carefully and fully considered but is not deemed persuasive. The reference does teach that the antigens are separated by SDS-PAGE electrophoresis and an antigen 'profile' may be generated. This was routine practice in the art at the time the invention was made.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 204-223 are rejected under 35 U.S.C. 103(a) as being unpatentable over (US 6,245,331) and Weiderkehr et al (Electrophoresis. 1991. 12: 478-486) in view of (US 5,116,766) and Kronberg et al (APMIS 100: 175-182, 1992).

US 6,245,331 teaches a method for the early detection of mycobacterial disease. Column 21, from line 8, describes a method for identifying and isolating early Mycobacterial antigens. This involves immunocapture using an adsorbed patient serum. Columns 22, from line 31 on, describes the detection of immune complexes

containing early Mycobacterium antigens suggesting that it is known to isolate complexes which can then be dissociated. See columns 17-18 for discussion of preferred immunoassays, such as ELISA and EIA. Columns 19-20 teach that direct and indirect agglutination assays may also be used. See column 21, lines 9-37 and column 22, lines 31-45.

Weiderkehr et al teach that the protein nature of soluble immune complexes (IC) from fresh plasma, cerebrospinal fluid (CSF), and urine was studied by combining several analytical and biochemical techniques. In plasma and CSF, free immunoglobulins G were separated from larger IC by gel filtration with a fast protein liquid chromatographic system. In urine, IC were separated by precipitation with polyethylene glycol. IC were further purified by protein-A and protein-G affinity chromatography and analyzed by two-dimensional gel elvctrophoresis. Apart from plasma samples from healthy donors, IC from cases with macrocreatine kinase type I and multiple sclerosis were analyzed. For CSF two cases of multiple sclerosis and for urine one case with urinary tract infection are shown. The method can be used for the examination of IC of unknown protein composition in body fluids. Elevated levels of circulating IC are frequently detected in body fluids of patients with infectious disorders, autoimmnune diseases, and in a variety of malignancies. Great efforts have been undertaken to develop and refine analytical means for identification and quantification of circulating IC. Normally they are measured in serum. Well-known examples with occasionally very high concentrations of IC are rheumatic disorders such as systemic lupus erythematosus (SLE) , SjOgrea's syndrome, rheumatoid arthritis, and ankylosing

spondylitis. Other examples are persistent infections such as viral hepatitis and secondary syphilis. A special group of disorders with circulating IC represents neurological diseases such as multiple sclerosis (MS), progressive rubella panencephalitis, subacute sclerosing panencephalitis, and amyotrophic lateral sclerosis (ALS). In many MS patients, IC are also found in cerebrospinal fluid (CSF).

However, Kronberg and US 6,245,331 don't particularly exemplify the separation of the immune complexes and identification of protein components.

The teachings of US 5,116,766 are set forth above. The reference relates to immune complex isolation and methods for diagnosing diseases. See abstract. Column 1 of the patent teaches that it was known to **isolate circulating immune complexes from sera by contacting the sera with a component that binds to the immune complexes and may be removed with them**. A reagent RhC is used to precipitate the immune complexes from serum. The immune complex with RhC can then be immobilized on a protein A column. The complexes are then eluted using glycine. **The antigens are separated by SDS-PAGE electrophoresis and an antigen 'profile' may be generated.** See "isolation of IC [Immune Complexes] bridging columns 9-10. See column 7, line 59-column 8, line 16 and Example 2. This clearly teaches obtaining an immune complex from a subject that has been elicited against said protein, and identifying it. It has already demonstrated that said protein is capable of raising an immune response as there is an antibody directed against it

Kronberg discloses the separation and identification of antigenic components of **immune complexes** in CF sputum using SDS-PAGE and immunoblotting. Immune

complexes were precipitated with PEG and then analyzed by SDS-PAGE before transfer to nitrocellulose. See abstract. Those transferred were probed with, among others, pooled sera from patients chronically infected with P.aeruginosa. Kronberg et al demonstrate the existence of immune complexes consisting of LPS and anti-LPs antibodies. See abstract and whole document.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to isolate any immune complex from a subject which has elicited an immune response to an antibody in order to form said immune complex as the prior art references cited above all teach the isolation of such ICs from samples. Additionally, isolating and identifying the components of these complexes would also have been obvious to one of ordinary skill in the art at the time the invention was made. US 5,116,766 specifically teaches that an antigen profile may be generated based on the proteins isolated/disassociated from the complex. Kronberg et al also teaches the isolation of antigens from antibodies in an immune complex. The use of gel electrophoresis, Mass spectrometry, and dissociating agents for these methods is consistent with the prior art references and what was known in the prior art at the time the invention was made.

Status of claims:

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

12/3/10